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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,495	06/24/2005	Geoffrey Lee	66741-039	5458

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EXAMINER	
MAEWALL, SNIGDHA	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,495	LEE ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *15-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/04/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of IDS filed on 04/04/06 is acknowledged.

Restriction/Election

2. Applicant's election with traverse of Group 1, claims 1-14 in the reply filed on 12/18/07 is acknowledged.

Applicant's election of species as 5-aminolevulinic acid methyl ester, i.e., wherein R^1 is methyl group and each of R^2 are hydrogen atoms, and (2) polymer-acrylates is also acknowledged.

The traversal is on the ground(s) that the common technical feature uniting the claims is crystal ALA derivative of a size less than 200 micrometer. As discussed in paragraphs [0004] to [0008], this size limitation solves the problems of stability and low release speeds for ALA dermal application compositions in the art.

This is not found persuasive because the limitation of solving stability problem is not recited in claims and furthermore the claims are drawn to dermal application system wherein the intended use has no patentable weight. The prior art teaches aminolevulinic acid salts, therefore the claim lacks novelty and inventive step of the special technical feature. Like instant application, prior art also teaches that ALA salts are used in dermal applications.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention there being no allowable generic or linking claim. Accordingly, claims pending in the prosecution are claims **1-14.**

Claim Objections

3. Claims 3-4, 6-7, 9-10 and 13-14 are objected to under 37 CFR 1.75(c) as being in improper form because a ("multiple dependent claim") shall refer to such other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 discloses a general formula for ALA derivative; however, CH_2 group is missing from the formula. Examiner suggests rewriting the correct formula.

Claim1 recites the limitation “less than approximately” which makes the claim indefinite. It is not clear whether the limitation is less than or approximation.

Claim 10 recites the limitation "optionally" which makes the claim indefinite. It is not clear whether the limitation is really the limitation or not.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-6 and 8-14 are rejected Under 35 U.S.C. 103(a) as being unpatentable over WO 95/05813 (WO) in view of US 5,856,566 ('566).

WO, teaches pharmaceutical compositions comprising aminolevulinic acid (ALA) and its salt applied to skin or other dermal membrane, such as in the form of a skin patch (abstract and page 5, lines 20-35) for treating cutaneous conditions. WO teaches the composition is anhydrous. WO recognizes that ALA is unstable in fluid vehicles and degrades rapidly, particularly at higher pH (page 2, last paragraph). Like the instant disclosure, WO also desires a stable ALA preparation for dermal administration (page 3, L 5-20) and suggests adding a stabilizing amount of a solid carrier to prevent or minimize degradation of ALA (page 4, L 13-23). With respect to administration, WO teaches adhesive matrix and reservoir devices i.e., pressure sensitive adhesive matrix made of polymers such as acrylics, silicones etc (page 7-page 8). WO teaches incorporating 0.5% to 50% ALA in the matrix. WO also discloses that

ALA, in addition to the meaning given in the art, is used through out the application to refer to pharmaceutically acceptable salts of ALA, which are considered equivalent for purposes of this invention (see page 5, lines 20-25).

WO fails to teach crystalline ALA having a particle size of less than 200 microns.

'566 teaches ALA crystals for photodynamictherapy of actinic keratoses, hair removal and other conditions (abstract, col. 9, L 11-15). '566 recognize that ALA has a very short half-life and is also very sensitive to ambient conditions (col. 2, L 7-25), particularly, the fact that aqueous solutions of ALA degrade rapidly (also recognized by instant disclosure as well as WO). In order to overcome the degradation problem, '566 suggests employing micronized crystals of ALA (col. 2, L 45-53 and L 62-67; col. 4, L 43-53 and examples in col. 10). '566 further discloses that "5-Aminolevulinic acid is also known as 5-aminolaevulinic acid, .delta.-aminolevulinic acid, .delta.-aminolaevulinic acid and 5-amino-4-oxopentanoic acid. 5-Aminolevulinic acid can be used as the salt, particularly a simple salt and especially the hydrochloride salt. 5-Aminolevulinic acid can also be used in the form of a precursor or product of 5-aminolevulinic acid. 5-Aminolevulinic acid can also be used in its pharmacologically equivalent form, such as an amide or ester. Examples of precursors and products of 5-aminolevulinic acid and pharmacologically equivalent forms of 5-aminolevulinic acid that can be used in the present invention are described in J. Kloek et al., Prodrugs of 5-Aminolevulinic Acid for Photodynamic Therapy, Photochemistry and Photobiology, Vol. 64 No. 6, December 1996, pages 994-1000; WO 95/07077; Q. Peng et al., Build-Up of Esterified Aminolevulinic-Acid-Derivative-Induced Porphyrin Fluorescence in Normal Mouse Skin,

Journal of Photochemistry and Photobiology B: Biology, Vol. 34, No. 1, June 1996; and WO 94/06424, which are all incorporated by reference herein in their entirety. As used herein, all of these compounds, unless other wise noted, are referred to jointly and severally as "ALA." (see column 4, lines 5-30).

It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ crystalline ALA or derivatives thereof, in the transdermal compositions of WO because both '566 and WO desire a stable ALA preparation that does not degrade and while WO incorporates stabilizing amounts of carrier materials, '566 suggest crystals of ALA having sizes in micrometers, which are in addition to being stable are also sterile. Further, '566 suggest that the crystalline ALA particles can also be administered in the form of solutions without any degradation problems. Thus, a skilled artisan would have expected highly sterile and extremely stable ALA/ALA derivatives/salts crystals that can be successfully delivered at the desired site and in the desired amounts. '566 do not teach the exact particle size claimed. However, 566 suggests employing ALA crystals in microparticle sizes. Accordingly, optimizing the size range of ALA crystals that are added to the transdermal matrix system of WO, without losing the stability or activity of ALA/ALA derivative/salts would have been within the scope of a skilled artisan.

8. Claims 1-6 and 8-14 are rejected Under 35 U.S.C. 103(a) as being unpatentable over WO 95/05813 (WO) in view of US 5,856,566 ('566) and further in view of WO 97/10811 and US PG pub. 20040171881).

The teachings of WO 95/05813 (WO) in view of US 5,856,566 ('566) have been discussed above. With regard to the suitability of nano crystals, '881 discloses that nano crystalline formulations typically afford greater bioavailability of drug compounds (see paragraph [1426]) and WO '811 discloses the benefit of enhancing solubility and use of nano particles in photodynamic therapy (abstract title and page 3, first paragraph).

Motivated by the advantages of nano particles in photodynamic therapy and increase in bioavailability exhibited by nano crystalline drugs, it would have been obvious to one of ordinary skilled in the art at the time the invention was made to optimize the particle size of ALA/ALA derivatives as disclosed by WO '813 and result in the claimed invention with a reasonable expectation of success.

9. Claims 1-6 and 8-14 rejected under 35 U.S.C. 103(a) as being unpatentable over (WO 96/06602) in view of USP (5,856,566 A).

WO 96/06602 discloses compositions and methods of increased stability comprising ALA derivatives for the administration to the skin of a mammal. The formulation can be in the form of skin patch(abstract and title). The weight of ALA has been disclosed to be between 0.5 to 50% by weight (see page 10, lines 20-25).

Like the instant disclosure, WO also desires a stable ALA preparation for dermal administration (page 3, L 5-20) and suggests adding a stabilizing amount of a solid carrier to prevent or minimize degradation of ALA (page 4, L 13-23). With respect to administration, WO teaches adhesive matrix and reservoir devices i.e., pressure

sensitive adhesive matrix made of polymers such as acrylics, silicones etc (page 7-page 8). WO teaches incorporating 0.5% to 50% ALA in the matrix. WO also discloses that ALA, in addition to the meaning given in the art, is used through out the application to refer to pharmaceutically acceptable salts of ALA, which are considered equivalent for purposes of this invention (see page 5, lines 20-30).

WO fails to teach crystalline ALA having a particle size of less than 200 microns.

'566 teaches ALA crystals for photodynamictherapy of actinic keratoses, hair removal and other conditions (abstract, col. 9, L 11-15). '566 recognize that ALA has a very short half-life and is also very sensitive to ambient conditions (col. 2, L 7-25), particularly, the fact that aqueous solutions of ALA degrade rapidly (also recognized by instant disclosure as well as WO). In order to overcome the degradation problem, '566 suggests employing micronized crystals of ALA (col. 2, L 45-53 and L 62-67; col. 4, L 43-53 and examples in col. 10). '566 further discloses that "5-Aminolevulinic acid is also known as 5-aminolaevulinic acid, .delta.-aminolevulinic acid, .delta.-aminolaevulinic acid and 5-amino-4-oxopentanoic acid. 5-Aminolevulinic acid can be used as the salt, particularly a simple salt and especially the hydrochloride salt. 5-Aminolevulinic acid can also be used in the form of a precursor or product of 5-aminolevulinic acid. 5-Aminolevulinic acid can also be used in its pharmacologically equivalent form, such as an amide or ester. Examples of precursors and products of 5-aminolevulinic acid and pharmacologically equivalent forms of 5-aminolevulinic acid that can be used in the present invention are described in J. Kloek et al., Prodrugs of 5-Aminolevulinic Acid for Photodynamic Therapy, Photochemistry and Photobiology, Vol. 64 No. 6, December

1996, pages 994-1000; WO 95/07077; Q. Peng et al., Build-Up of Esterified Aminolevulinic-Acid-Derivative-Induced Porphyrin Fluorescence in Normal Mouse Skin, Journal of Photochemistry and Photobiology B: Biology, Vol. 34, No. 1, June 1996; and WO 94/06424, which are all incorporated by reference herein in their entirety. As used herein, all of these compounds, unless other wise noted, are referred to jointly and severally as "ALA." (see column 4, lines 5-30).

It would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ crystalline ALA or derivatives thereof, in the transdermal compositions of WO because both '566 and WO desire a stable ALA preparation that does not degrade and while WO incorporates stabilizing amounts of carrier materials, '566 suggest crystals of ALA having sizes in micrometers, which are in addition to being stable are also sterile. Further, '566 suggest that the crystalline ALA particles can also be administered in the form of solutions without any degradation problems. Thus, a skilled artisan would have expected highly sterile and extremely stable ALA/ALA derivatives/salts crystals that can be successfully delivered at the desired site and in the desired amounts. '566 do not teach the exact particle size claimed. However, 566 suggests employing ALA crystals in microparticle sizes. Accordingly, optimizing the size range of ALA crystals that are added to the transdermal matrix system of WO, without losing the stability or activity of ALA/ALA derivative/salts would have been within the scope of a skilled artisan.

10. Claims 1-6 and 8-14 are rejected Under 35 U.S.C. 103(a) as being unpatentable over WO 96/06602 in view of US 5,856,566 ('566) and further in view of WO 97/10811 and US PG pub. 20040171881).

The teachings of WO 96/06602 (WO) in view of US 5,856,566 ('566) have been discussed above. With regard to the suitability of nano crystals, '881 discloses that nano crystalline formulations typically afford greater bioavailability of drug compounds (see paragraph [1426]) and WO '811 discloses the benefit of enhancing solubility and use of nano particles in photodynamic therapy (abstract title and page 3, first paragraph).

Motivated by the advantages of nano particles in photodynamic therapy and increase in bioavailability exhibited by nano crystalline drugs, it would have been obvious to one of ordinary skilled in the art at the time the invention was made to optimize the particle size of ALA/ALA derivatives as disclosed by WO '813 and result in the claimed invention with a reasonable expectation of success.

11. Claim 7 is rejected Under 35 U.S.C. 103(a) as being unpatentable over (WO 96/06602 or WO 95/05813 (WO) in view of US 5,856,566 ('566), WO 97/10811 and US PG pub. 2004/0171881) and further in view of US 5,456,745 ('745).

'566 discussed above fail to teach the claimed polymer and softener. WO teaches acrylic polymers such as Eudragit but does not teach the softener, '745 teach a flexible film forming gels made of polymeric materials such as Eudragit, cellulose, gums etc 9co1.2, L 19-67) containing moisturizers, softeners such

as citric acid esters (col. 3, L 65-67) etc., and exhibits adhesive properties (col. 6, L 46-54, col. 9, L 37-60). '745 teach employing skin treatment agents in the gel films for providing treatment to skin conditions such as acne, psoriasis etc (col. 8). Thus, polymer matrix made of claimed acrylate polymers containing softeners such as citrate esters are known in the art. Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to include softeners such as citrate esters, moisturizers etc., in the polymeric matrix materials that constitute the adhesives of WO containing the crystals of ALA ('566) with an expectation provide a flexible polymer comprising ALA crystals such that the polymer matrix is stable and also easy to handle. Further, preparing the matrix containing citrate and ALA by employing the suitable steps would have been within the scope of a skilled artisan.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/

Primary Examiner, Art Unit 1612

/Snigdha Maewall/
Examiner, Art Unit 1612